nature structural & molecular biology

SUPPLEMENTARY INFORMATION

In the format provided by the authors and unedited.

Phase separation drives X-chromosome inactivation: a hypothesis

Andrea Cerase[1,7,8*], Alexandros Armaos[2,8], Christoph Neumayer[3], Philip Avner[1], Mitchell Guttman[3*] and Gian Gaetano Tartaglia[2,4,5,6*]

[1]EMBL-Rome, Monterotondo, Italy. [2]Centre for Genomic Regulation (CRG), The Barcelona Institute of Science and Technology, Barcelona, Spain. [3]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA, USA. [4]ICREA and UPF, Barcelona, Spain. [5]Department of Biology 'Charles Darwin', Sapienza University of Rome, Rome, Italy. [6]Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genoa, Italy. [7]Present address: Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK. [8]These authors contributed equally: Andrea Cerase, Alexandros Armaos. *e-mail: a.cerase@qmul.ac.uk; mguttman@lncrna.caltech.edu; gian.tartaglia@crg.eu

Supplementary Table 1. (A) *Xist partners from proteomic and genetic studies.* The table indicates if the listed proteins occur in the studies referenced as stress granule components (constitutive components, '*Stress Granule (core)'* or found in the assembly '*Stress Granule (known)'*), paraspeckle elements ('*Paraspeckles*') or *Neat1* interactors ('*Neat1 Interactors'*). Occurrence is indicated as 1=presence or 0=absence. **(B)** *cat*RAPID *Global Score* predictions (*I*) for protein interacting with *Xist.* Additional annotations refer to proteins predicted to contain intrinsically disordered regions (*IDR, P=positive* and *N=negative*) and the degree of disorder confidence (DC) (*cleverMachine;* https://goo.gl/GKX8c4) as well as liquid-liquid phase separation propensity (LLPS) (*cat*GRANULE; https://goo.gl/5KkVkM); (**C**, **D, E, F, G**) same as **(B)** for each of *Xist* interactor reported in Minajigi, A. *et al. Science* 349, aab2276 (2015) (**C**), Chu, C. *et al. Cell* 161, 404-416 (2015) (**D**), McHugh, C. A. *et al. Nature* 521, 232-236 (2015) (**E**), Moindrot, B. *et al. Cell reports* 12, 562-572 (2015) (**F**), Monfort, A. *et al. Cell reports* 12, 554-561 (2015) (**G**).

All the comparisons reported in the main text were carried out using values of the table. The statistical significance was assessed through Fisher's test (one-side test; no multiple comparisons needed). The following datasets were employed: 236 constitutive components of stress granules for the comparison of granule-forming proteins and *Xist* interactome, 1486 RNA-binding proteins for the analysis of *Neat1* and *Xist* interactomes, and 3175 structurally disorder proteins for the overlap between disordered proteins and *Xist* interactome. In total, 14 out of 37 *Xist* direct interactors are also *Neat1* interactors; p-value $<10^{-6}$, 20 out of 37 *Xist* direct interactors are stress granule components; p-value: 10^{-6} and 15 out of 37 *Xist* direct interactors are predicted to be highly disordered with a confidence of 100%; p-value: $7x10^{-5}$.